IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences

AF 1623 #21 10-6-00

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In re Patent Application of

Reid W. von Borstel, et al

Serial No. 08/463,740

Filed: June 5, 1995

Atty Dkt.: 1331-143
C# M#

Group Art Unit: 1623

Examiner: Owens, H.

Date: October 2, 2000

Title: PYRIMIDINE NUCLEOTIDE PRECURSORS FOR TREATMENT OF SYSTEMIC INFLAMMATION AND INFLAMMATORY HEPATITIS

Honorable Commissioner for Patents and Trademarks
Washington, DC 20231

Sir:

☐	**NOTICE OF APPEAL** Applicant hereby appeals to the Board of Appeals from the decision dated _____ of the Examiner twice/finally rejecting claims _____ ($ 300.00)	$	0.00
☐	An appeal **BRIEF** is attached in triplicate in the pending appeal of the above-identified application ($ 300.00)	$	0.00
☐	An **ORAL HEARING** is requested under Rule 194 ($ 260.00) (due within two months after Examiner's Answer)	$	0.00
☐	Credit for fees paid in prior appeal without decision on merits	-$ (	0.00)
☒	A reply brief is attached in triplicate under Rule 193(b)		**(no fee)**
☐	Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s) **($110.00/1 month**; $380.00/2 months; **$870.00/3 months**; $1,360.00/4 months)	$	0.00
	SUBTOTAL	$	0.00
☒	Applicant is a "small entity"; enter ½ of subtotal and subtract ☐ "small entity" statement attached	-$(	0.00)
	SUBTOTAL	$	0.00
	Less month extension previously paid on	-$(	0.00)
	TOTAL FEE ENCLOSED	$	0.00

Any future submission requiring an extension of time is hereby stated to include a petition for such time extension. The Commissioner is hereby authorized to charge any deficiency in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our **Account No. 14-1140.** A duplicate copy of this sheet is attached.

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NIXON & VANDERHYE P.C.
By Atty: Leonard C. Mitchard, Reg. No. 29,009

Signature: _____

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In re Patent Application of
von BORSTEL et al
Serial No. **08/463,740**
Filed: **June 5, 1995**

Atty. Ref.: **1331-143**
Group: **1623**
Examiner: **Owens, H.**

For: **PYRIMIDINE NUCLEOTIDE PRECURSORS FOR TREATMENT OF SYSTEMIC INFLAMMATION AND INFLAMMATORY HEPATITIS**

* *

October 2, 2000

Honorable Commissioner of Patents
and Trademarks
Washington, DC 20231

REPLY BRIEF

Sir:

Applicant hereby replies to the Examiner's Answer mailed August 2, 2000.

The Examiner asserts in the Answer that the Brief does not contain a statement identifying related appeals and interferences. This is not correct. At the top of page 2 of the Brief, the following appears

"RELATED APPEALS AND INTERFERENCES

The appellant, the undersigned, and the assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal."

The Examiner continues to assert that the claimed compositions are *prima facie* obvious. This position is respectfully traversed.

The invention relates to generally to pyrimidine nucleotide precursors, including acyl derivatives of cytidine, uridine and orotic acid, and to the prophylactic and therapeutic uses of these compounds. The compositions are effective in improving survival and in preventing tissue damage from SIRS, including sepsis. The claimed pharmaceutical compositions comprise an acyl derivative of uridine, cytidine or orotic acid and an inhibitor of uridine phosphorylase.

The sole rejection is that of alleged obviousness of Claims 41 and 58 - 67 under 35 USC 103 over von Borstel et al. in view of Chu et al. for the reasons already of record on pages 2 - 3 of the Office action mailed April 2, 1996. The Examiner asserts:

> "Given that Von Borstel et al. sets forth a composition for increasing serum and intracellular free uridine, one of skill in the art would have a reasonable expectation of success that a further component, specifically a uridine phosphorylase inhibitor which has been shown in the prior art to reduce the degradation of uridine to uracil, would be advantageous as an additional

component for increasing or at the very least maintaining the availability of free uridine. Thus, the claimed compositions are *prima facie* obvious in the absence of clear and convincing evidence to the contrary."

Claim 41 is directed to a composition comprising (a) an acyl derivative of uridine, cytidine or orotic acid, and (b) an inhibitor of uridine phosphorylase. The remaining claims in the case (Claims 58-67) are composition claims which are dependent, either directly or indirectly, on Claim 41.

Von Borstel describes acylated derivatives of uridine and cytidine. There is no disclosure or suggestion in that reference of compositions comprising an acyl derivative of uridine, cytidine or orotic acid and an inhibitor of uridine phosphorylase.

Chu et al. relates principally to the treatment of cancer, and has nothing to do with compositions suitable for use in the treatment of inflammatory disorders. Chu et al describes the use of hydroxymethyl derivatives of 5-benzylacyclouridine and 5-benzoyloxybenzylacyclouridine in the potentiation of pyrimidine nucleosides, such as 5-fluoro-2'-deoxyuridine (FdUrd), in cancer chemotherapy by way of uridine phosphorylase inhibition. The focus of Chu et al is to **prevent the cleavage of the**

nucleoside analog to a less effective material, and **not** to elevate uridine levels. As noted at column 1, lines 15 through 17 of Chu et al:

> "The efficacy of the chemotherapeutic agent FdUrd is limited by its **cleavage** the less effective base 5-fluorouracil (FUra)." (Emphasis added)

Chu et a further states at column 3, line 67:

> "A specific object of the present invention is to provide novel uridine phosphorylase inhibitors which reduce **phosphorolytic degradation** of FdUrd to the less active FUra in tumor cells." (Emphasis added)

The Examiner asserts that one of ordinary skill would have a "reasonable expectation of success" based on the cited disclosures, that incorporating a further component (a uridine phosphorylase inhibitor) would be advantageous. It not seen how such expectation could possibly arise in the mind of a person of ordinary skill in view of the disclosures of the cited references. Chu et al relates to the treatment of cancer and is premised on the prevention of degradation of **FdUrd to the less active FUra** in tumor cells. Von Borstel describes **acylated** derivatives of uridine and cytidine, and provides no suggestion of compositions comprising an **acyl** derivative of uridine, cytidine or orotic acid and an inhibitor of uridine phosphorylase. It is believed therefore that a person of ordinary skill would **not** have experienced the expectation of success assumed by the Examiner based on the

combined disclosures of von Borstel et al and Chu et al. Absent any such expectation, there would have been no motivation to combine the cited disclosures. No *prima facie* case of obviousness has therefore been established in this case.

For the above reasons, reversal of the obviousness rejection is believed to be in order. Such action is respectfully requested.

CONCLUSION

In conclusion it is believed that the present application is in clear condition for allowance. Reversal of the Final Rejection and passage of the subject application to issue are earnestly solicited.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

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